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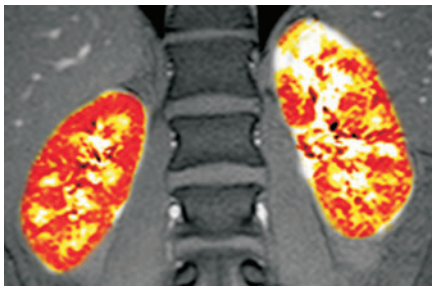
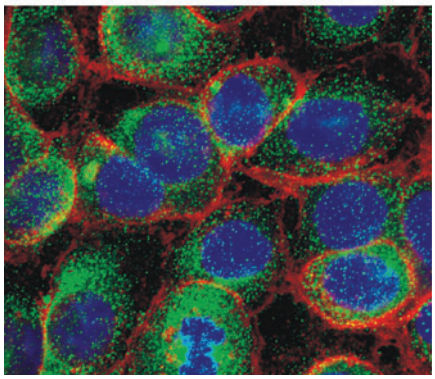
BOLD MRI: a new renal imaging method



Ischemia and hypoxia are two of the major causes of acute renal failure. Yet measurement of tissue oxygen tension in a noninvasive manner was not possible until recently. Two groups of investigators report in this issue on a noninvasive evaluation of renal oxygenation using blood oxygenation level-dependent magnetic resonance imaging (BOLD MRI) in normal subjects and in those exposed to potential nephrotoxins. In one paper (**see page 144**), normal, healthy volunteers were given indomethacin, an iodinated radio-contrast medium such as iopromidum, or the calcineurin inhibitors cyclosporine micro-emulsion and tracrolimus. Using this method, cortical and medullary oxygenation could be evaluated. The contrast agent reduced medullary renal oxygenation, whereas cyclosporine increased it. Indomethacin and tacrolimus had no effect on medullary renal oxygenation. In the second study (**see page 139**), the effect of water diuresis was investigated in healthy volunteers before and after treatment with naproxen. BOLD MRI revealed that water diuresis increased renal medullary oxygenation before treatment with naproxen. Pretreatment with naproxen negated the response of BOLD MRI to water diuresis. The flow rate responses in subjects were variable, but the temporal responses were more consistent. These studies suggest that BOLD MRI could have a wide application in the study of nephrotoxicity of established and new therapeutic agents.

Factor H and membranoproliferative glomerulonephritis

The deposits in the basement membrane of patients with dense deposit disease (a form of membranoproliferative glomerulonephritis) often contain complement. At least three mechanisms have been found to lead to complement deposition. In one mechanism, Factor H is absent. The second is the inactivation of Factor H by a circulating inhibitor. The third mechanism is the presence of the autoantibody C3 nephritic factor. In this issue, Zipfel and colleagues report on a potential fourth mechanism. They studied two sisters (daughters of a consanguineous marriage) with deletion of a single lysine residue within one of the complement regulatory domains of Factor H. Mutant Factor H was purified from the patient's plasma and was found to have reduced decay-accelerating activity and binding complement component C3b. However, other functions of Factor H, such as binding to cells, were equal to those in the normal protein. Interestingly, the patients and their healthy mother were positive for C3 nephritic factor autoantibody. Treatment with fresh frozen plasma was well tolerated and prevented disease progression. It is expected to preserve kidney function. **See page 42**.



Role of maxi-K channels in Bartter's syndrome

Recent studies on the genetics of Bartter's syndrome have identified many subtypes of this interesting disease, each of which is associated with a specific mutation of one of the transporters of electrolyte absorption or secretion in the thick ascending limb. The type II variety, a hypokalemic renal salt-wasting disorder, is caused by mutations in the renal outer medullary potassium (ROMK) channel. The ROMK channel mediates K recycling in the thick ascending limb of Henle's loop but is also responsible for K secretion in the distal nephron. Newborn patients have an initial hyperkalemia compatible with the loss of K secretion in the distal nephron, but the mechanism by which these infants rapidly develop hypokalemia as they get older is not known. In this issue, Hebert and colleagues provide an explanation of this puzzle. The authors studied mice with deletions of this ROMK channel. They found that, as expected, K absorption in the loop of Henle was reduced and could account for some of the renal potassium wasting. Surprisingly, they found sustained K secretion in the collecting tubule, which was stimulated by urine flow rate. Finally, the characteristics of the channel were most compatible with the maxi-K channel. **See page 51**.